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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Christoph Reinhard et al.
Application No.	: 09/905,674
Filed	: July 13, 2001
For	: TETRASPAN PROTEIN AND USES THEREOF
Examiner	: Karen A. Lacourciere
Art Unit	: 1635
Docket No.	: 59516-7 / PP-01700.002
Date	: March 19, 2004

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Commissioner for Patents
P.O. Box 1450
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DECLARATION OF DR. CHRISTOPH REINHARD UNDER 37 C.F.R. § 1.132
(IN SUPPORT OF RESPONSE UNDER 37 C.F.R. § 1.116)

Sir:

I, Dr. Christoph Reinhard, being duly sworn, say:

1. I am a true and original inventor of the claimed subject matter of the above-identified patent application.

2. I am an internationally recognized scientist and am presently employed as a Project Leader at Chiron Corporation, Emeryville, California (Employed at Chiron from 1995 to present). I received a Bachelors Degree in Human Genetics from the Universitat Frieburg and a

Ph.D. degree from the Friedrich Miescher Institute in Biochemistry.

3. I am an author or co-author of more than 17 peer-reviewed research articles and have been invited to give numerous presentations on my research at national and international meetings. My curriculum vitae is attached.

4. In my capacity as a biochemist and molecular biologist, I am familiar with identifying and characterizing proteins, based on homology (both sequence alignment and structural homology), using algorithms and methods well-known to those of ordinary skill in the art at the time of filing of the above-identified patent application.

5. I understand that claims of the above-referenced patent application are rejected under 35 U.S.C. § 112, first paragraph, on the grounds that one skilled in the art would not know how to use the claimed invention, because the claimed invention is allegedly not enabled. I generally understand that enablement refers to whether one skilled in the art can make and/or use the invention as claimed.

6. SEQ ID NO:2 shares substantial and highly characteristic homologies with tetraspan proteins. Tetraspan proteins are disclosed in Serru *et al.* (Biochim Biophys Acta. 2000 Mar 16;1478(1):159-63) and Maecker *et a.l* (FASEB J. 1997 May;11(6):428-42). The following Table I summarizes these *substantial and highly characteristic* structural homologies:

TABLE I. Structural Homology between SEQ ID NO:2 and Tetraspan Proteins

TETRASPAN PROTEIN FEATURES	SEQ ID NO:2
Presence of four hydrophobic transmembrane (TM) domains	YES: TM-1 at aa 18-39 TM-2 at aa 59-84 TM-3 at aa 89-115 TM-4 at aa 233-255
Presence of two hydrophilic loop regions	
Small hydrophilic loop region between TM-1 and TM-2; 14-29 aa in length	YES: Hydrophilic region at aa 40-58 between TM-1 and TM-2; 18 aa in length
Large hydrophilic loop region between TM-3 and TM-4; 68-109 aa in length	YES: Hydrophilic region at aa 116-232 between TM-3 and TM-4; 116 aa in length (slightly longer than most tetraspan proteins)
Presence of putative N-linked glycosylation site in large hydrophilic loop region (consensus: NXS/T where X is not Pro)	YES: NCS sequence at aa 169 in large hydrophilic loop region
Presence of conserved Lys just before TM-1	YES: Lys residue at aa 16; 2 aa before start of TM-1
Presence of conserved polar amino acids within transmembrane domains	
Asn in TM-1	YES: Asn at aa 23 (within TM-1)
Glu or Gln in TM-3 and TM-4	YES: Glu at aa 105 (within TM-3); Gln at aa 247 (within TM-4)
Presence of four conserved Cys residues in large hydrophilic loop region	
CCG motif 50 aa downstream of TM-3	YES: CCG at aa 153 (38 aa downstream of TM-3)
Cys preceded by Gly 11 aa upstream of TM-4	YES: Cys preceded by Gly at aa 241 (exactly 11 aa upstream of TM-4)
Variably placed Cys in PXSC motif	YES: PFSC sequence at aa 183

6. Therefore, a person of ordinary skill in the art would reasonably conclude that the present polypeptide of SEQ ID NO:2 is a member of the tetraspan family of proteins with activities reflective thereof. Significantly, this conclusion is based not only on the ***high degree of amino acid sequence identity*** with tetraspan protein, but also on the ***substantial, and highly characteristic*** structural homology presented herein above in view of the ***structural hallmarks*** of this protein family (as discussed by Serru *et al.* and Maecker *et al.*).

7. In conclusion, knowledge, techniques and reagents available as of the time of filing of the above-identified patent application, including substantial **sequence identity and** substantial **structural homology**, demonstrate that the present polypeptide of SEQ ID NO:2 is a functional member of the tetraspan family of proteins.

8. I further declare that all statements made herein of my own knowledge are true and that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code.

C. Reinhard 03/22/04

Christoph Reinhard